



# **FDA-Approved Treatments for Schizophrenia**

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# Schizophrenia in a Nutshell

## What is schizophrenia?

- A chronic, severe, and disabling mental disorder that impacts a person's thoughts, feelings, and behaviors. It is characterized by a distorted perception of reality, which can manifest in a range of positive, negative, and cognitive symptoms. Individuals with schizophrenia may experience hallucinations, delusions, disorganized thinking, and a profound disconnection from reality, which significantly impairs their ability to function in everyday life.
- A patient must experience at least two symptoms, with at least one symptom being a positive symptom, within a period of at least six months.
- Schizophrenia typically begins in late adolescence or early adulthood and often persists for life.



# Symptoms of schizophrenia

- **Positive Symptoms**

These are symptoms that reflect an excess or distortion of normal functioning:

- Hallucinations: Perceptions without external stimuli, most commonly auditory hallucinations.
- Delusions: False beliefs that are resistant to reasoning or contrary evidence
- Disorganized thinking: Incoherent speech or thoughts, making it difficult for the person to communicate effectively.
- Disorganized or abnormal motor behavior: ranging from unpredictable agitation to catatonia

- **Negative Symptoms**

These reflect a diminution or loss of normal functioning:

- Anhedonia: Loss of interest or pleasure in activities that were once enjoyable.
- Flat Affect: Reduced emotional expression
- Avolition: Decreased motivation to initiate and sustain purposeful activities
- Alogia: A reduced ability to express oneself.

- **Cognitive Symptoms**

These symptoms primarily affect the mental processes necessary for learning and daily functioning:

- Impaired Working Memory
- Attention Deficits
- Executive Dysfunction

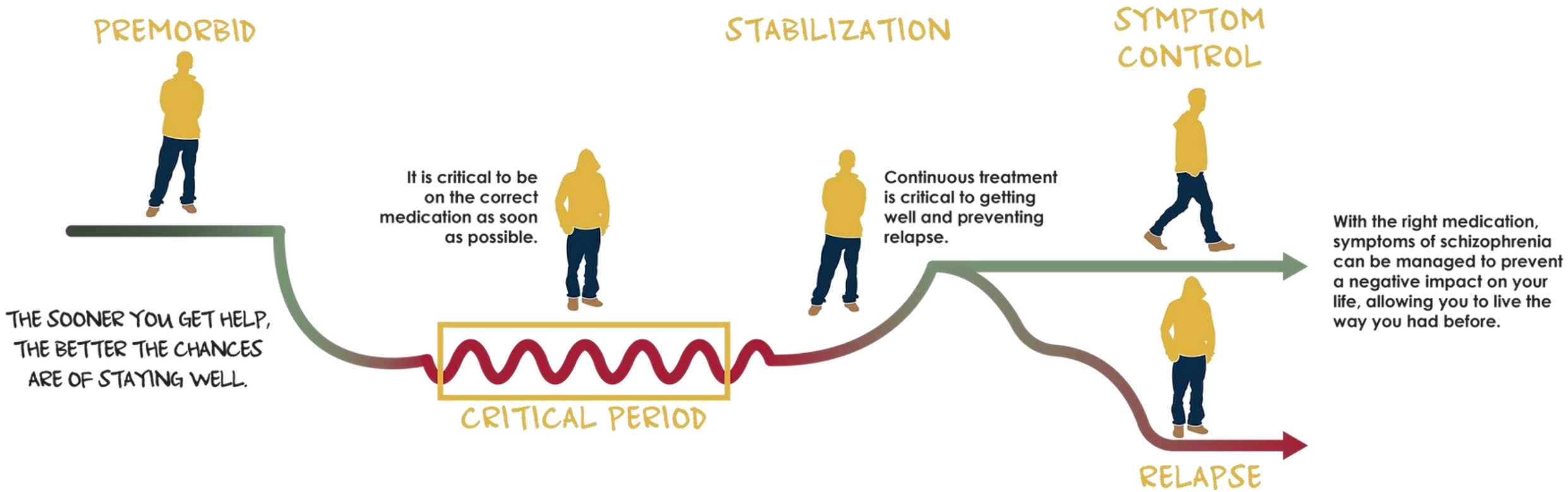


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# Goals of Treatment

- **Symptom reduction:** Alleviating hallucinations, delusions, and cognitive impairment.
- **Functional improvement:** Enhancing the ability to work, study, and interact socially.
- **Prevent relapse:** Minimizing hospitalizations and long-term disability.
- **Long-term management:** Ensuring medication adherence and addressing side effects.





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# FDA-Approved Treatments

- **Medications:** Antipsychotics (primary treatment)
- **Therapies:** Psychosocial interventions, Cognitive Behavioral Therapy (CBT), and family education.
- **Electroconvulsive Therapy (ECT):** For treatment-resistant schizophrenia.



# Common First-Generation (Typical) Antipsychotics

- **Haloperidol (Haldol)**

- FDA Approval: 1967
- Mechanism of action: Strong D2 receptor antagonism.
- Side Effects: High risk of EPS, sedation, orthostatic hypotension. Long-term use may lead to tardive dyskinesia.

- **Chlorpromazine (Thorazine)**

- FDA Approval: 1954
- Mechanism of action: Dopamine receptor antagonist.
- Side Effects: Sedation, hypotension, weight gain, and anticholinergic effects

Not first choice due to side effect profile



# Common Second-Generation Antipsychotics

- **Risperidone (Risperdal)**

- FDA Approval: 1993
- Mechanism of action: Potent D2 receptor and 5HT2A receptor antagonist.
- Side Effects: Sedation, weight gain, increased prolactin levels, sexual dysfunction.

- **Olanzapine (Zyprexa)**

- FDA Approval: 1996
- Mechanism of action: D2 and 5HT2A antagonist, with antihistaminergic effects.
- Side Effects: Significant weight gain, metabolic syndrome (elevated glucose, dyslipidemia), sedation.

- **Clozapine (Clozaril)**

- FDA Approval: 1989
- Mechanism of action: Antagonism of D1, D2, 5HT2A, and other receptors.
- Side Effects: Agranulocytosis (requiring regular blood monitoring), sedation, weight gain, metabolic side effects. Clozapine is highly effective for reducing suicidal behavior in schizophrenia patients.

- **Aripiprazole (Abilify)**

- FDA Approval: 2002
- Mechanism of action: Partial agonist at D2 and 5HT1A receptors, antagonist at 5HT2A receptors.
- Side Effects: Insomnia, restlessness (akathisia), anxiety, minimal weight gain compared to other SGAs.

- **Quetiapine (Seroquel)**

- FDA Approval: 1997
- Mechanism of action: D2 and 5HT2A antagonism, sedative properties.
- Side Effects: Sedation, weight gain, metabolic issues, orthostatic hypotension.



# Recent Developments in Antipsychotic Treatments

- **Brexipiprazole (Rexulti)**

- FDA Approval: 2015
- Mechanism of action: Partial agonist at D2 and 5HT1A receptors, antagonist at 5HT2A receptors.
- Side Effects: Weight gain, sedation, increased prolactin levels.

- **Cariprazine (Vraylar)**

- FDA Approval: 2015
- Mechanism of action: Partial agonist at D2 and D3 receptors, antagonist at 5HT2A receptors.
- Side Effects: Akathisia, insomnia, weight gain, sedation.

- **Long-Acting Injectables (LAIs)**

- Examples: Paliperidone palmitate (Invega Sustenna), Aripiprazole lauroxil (Aristada).
- Advantages: Improved adherence
- Side Effects: Common side effects are similar to oral antipsychotics, but LAIs can cause injection site reactions.

# Non-Pharmacologic Treatment Options

- Cognitive Behavioral Therapy (CBT)
  - Helps manage psychotic symptoms and reduce relapse rates by targeting delusions, hallucinations, and disorganized thinking.
  - Evidence: CBT has been shown to reduce the intensity of symptoms and improve quality of life.
- Family Intervention and Psychoeducation
  - Key for improving medication adherence and supporting families in coping with the challenges of schizophrenia.
  - Evidence: Family psychoeducation has been shown to reduce relapse rates and improve overall patient outcomes.
- Electroconvulsive Therapy (ECT)
  - Considered for treatment-resistant schizophrenia, particularly in patients who are severely symptomatic or have co-occurring mood disorders.
  - Evidence: ECT can be highly effective for patients who fail to respond to pharmacotherapy.



ELECTROCONVULSIVE THERAPY  
(ECT)

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# Future Directions in Schizophrenia Treatment

- **Personalized Medicine**

- Ongoing research aims to better match treatments with individual genetic profiles, enhancing efficacy and minimizing side effects.

- **New Drug Classes**

- Investigational treatments include glutamate modulators and novel dopamine-serotonin agents that may offer new mechanisms



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